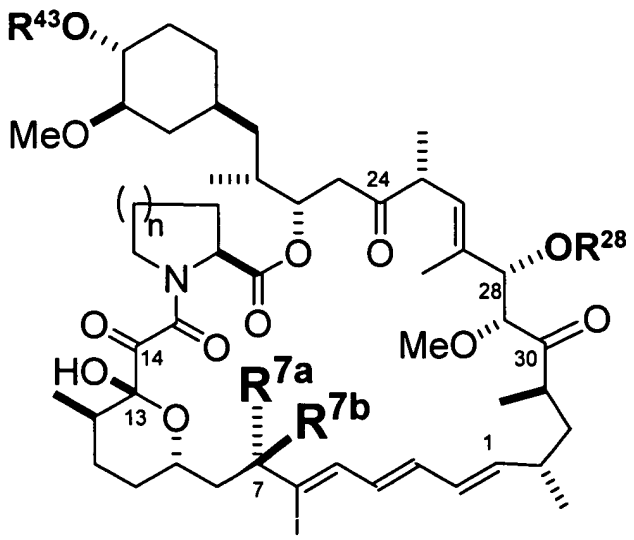
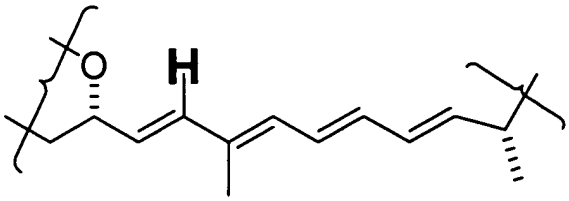


wherein

n is 1 or 2;

R^{28} and R^{43} are independently selected from the group consisting of H and a substituted or unsubstituted aliphatic or acyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO2R^A$, or $-NR^BSO2NR^AR^{B'}$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or a substituted or unsubstituted aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or a substituted or unsubstituted aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where a heteroaliphatic moiety is an aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

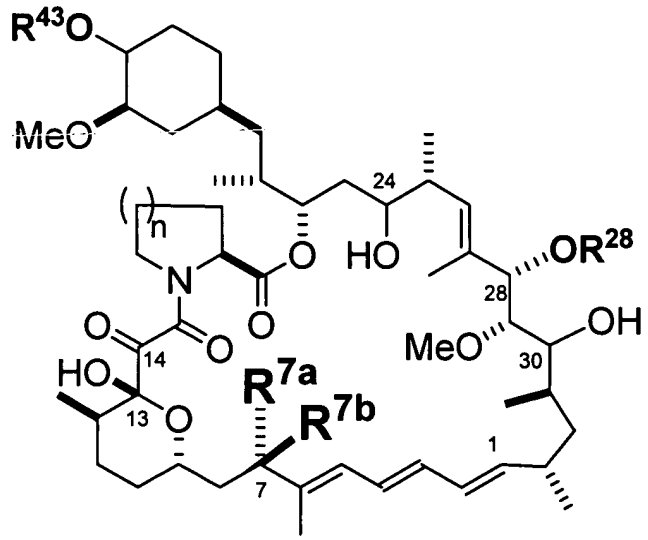
where an aryl moiety is a mono- or polycyclic unsaturated moiety having 3-14 carbon atoms; and

where a heteroaryl moiety is a mono- or polyheterocyclic unsaturated moiety having 3-14 carbon atoms;

or a pharmaceutically acceptable salt, ester, carbamate, metabolite or pro-drug thereof;

or a pharmaceutically acceptable salt of such ester or carbamate.

20. **(Twice amended)** A compound of the formula:

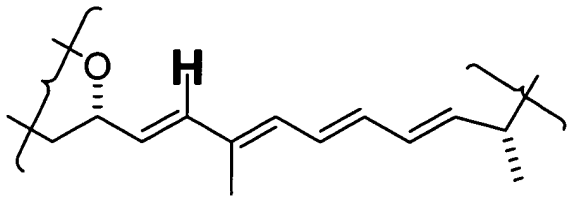


wherein

n is 1 or 2;

R^{28} and R^{43} are independently selected from the group consisting of H and a substituted or unsubstituted aliphatic or acyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO2R^A$, or $-NR^BSO2NR^AR^{B'}$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or a substituted or unsubstituted aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or a substituted or unsubstituted aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where a heteroaliphatic moiety is an aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where an aryl moiety is a mono- or polycyclic unsaturated moiety having 3-14 carbon atoms; and

where a heteroaryl moiety is a mono- or polyheterocyclic unsaturated moiety having 3-14 carbon atoms;

or a pharmaceutically acceptable salt, ester, carbamate, metabolite or pro-drug thereof;

or a pharmaceutically acceptable salt of such ester or carbamate.

42. **(Once amended)** A method for producing a compound of claim 1 which comprises contacting a homologous C28 epimer with a titanium tetraalkoxide reagent under suitable conditions and for a sufficient time to permit epimerization.

45. **(Once amended)** The method of any of claims 42-44 wherein the homologous C28 epimer is rapamycin.

Remarks

Applicants respectfully submit that the present Amendment and following Remarks remove all grounds for rejection of the application, thereby placing it in condition for allowance. In the Advisory Action mailed March 12, 2003, the Examiner indicated that the Amendment presented February 26, 2003, which is identical to the current Amendment, would not be entered, on the ground that it was not deemed to place the application in better form for appeal. The Examiner argued the amended claims would remain indefinite for three reasons, each of which is addressed individually below.

"Acyl":

The Examiner has maintained his position that the term "acyl" is indefinite, but has offered no argument or evidence to rebut Applicant's point that the term, though broad, is not at